Dear Sir,

We thank Mrs Stratton for highlighting that the figure of 0.7% for the self-reported history of measles infection in UK Biobank participants[1] is far lower than the likely true prevalence in this cohort.

Most UK Biobank participants were born between 1937-1970, and routine measles vaccination[2] in the UK began in 1968. Thus, most participants would not have been vaccinated against measles during childhood. Prior to vaccination, ~99% of children were seropositive for measles antibodies, suggesting that exposure to the virus was ubiquitous[2].

Self-reported measles infection was calculated from the following two interview questions, firstly, "*Has a doctor ever told you that you have had any other serious medical conditions or disabilities?*" [the "other" referring to cancer, which was discussed separately during the interview], and secondly, "*In the touch screen you selected that you have been told by a doctor that you have other serious illnesses or disabilities, could you now tell me what they are?*". We suspect the phrase "*serious medical conditions*" contributed to the low self-reports of measles, since for most participants a measles infection may not have been perceived as serious.

We observed[1] that high myopia was more common in participants who did vs. did not report having measles before age 17 years (OR=1.48, 95% CI 1.07–2.07). Since childhood measles infection was nearly ubiquitous, this association is likely reflects, in reality, an association between high myopia and an unusually serious or debilitating measles infection. In support of this we saw similar associations with reports of certain other febrile illnesses.

Self-report is a widespread tool in epidemiology, with recognised strengths and limitations[3]. Accuracy can range widely, e.g. sensitivity 83% for cataract and 31% for colon polyps in NHANES[4]. We hypothesize that reports for a severe childhood febrile illness are likely to be highly specific, but relatively insensitive. Such misclassification bias is likely to have reduced the power of our analyses. Methods to detect antibodies to viruses, e.g. VirScan[5], would provide greater accuracy.

We are grateful to Mrs Stratton for flagging this important point relating to the strengths and weaknesses of analyses using large population studies.

References

1. Guggenheim JA, Williams C, UK Biobank Eye and Vision Consortium. Childhood febrile illness and the risk of myopia in UK Biobank participants. *Eye* 2016; **30**: 608–614.
2. Fine PEM, Clarkson JA. Measles in England and Wales—II: The Impact of the Measles Vaccination Programme on the Distribution of Immunity in the Population. *Int J Epidemiol* 1982; **11**: 15-25.
3. Harlow SD, Linet MS. Agreement between questionnaire data and medical records. The evidence for accuracy of recall. *Am J Epidemiol* 1989; **129**: 233-248.
4. Bergmann MM, Byers T, Freedman DS, Mokdad A. Validity of Self-reported Diagnoses Leading to Hospitalization: A Comparison of Self-reports with Hospital Records in a Prospective Study of American Adults. *Am J Epidemiol* 1998; **147**: 969-977.
5. Xu GJ, Kula T, Xu Q, Li MZ, Vernon SD, Ndung'u T*, et al.* Comprehensive serological profiling of human populations using a synthetic human virome. *Science* 2015; **348**: doi: 10.1126/science.aaa0698.

Authors:

Jeremy A. Guggenheim[1] and Cathy Williams[2]

Affiliations:

1. School of Optometry & Vision Sciences, Cardiff University, Cardiff, UK.
2. School of Social and Community Medicine, University of Bristol, Bristol, UK.